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FINAL REPORT

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CYTOKINES AND IMMUNE SURVEILLANCE IN HUMANS

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INTRODUCTION

In view of the relocation of the principal investigator, Dr. Gerald Sonnenfeld, from the University of Louisville to the Carolinas Medical Center, this final report for work carried out at the University of Louisville is being prepared to facilitate transfer of the project to the Carolinas Medical Center.

Evidence from both human and rodent studies has indicated that alterations in immunological parameters occur after space flight [1,2]. Among the parameters shown, by us and others, to be affected is the production of interferons [1-3]. Interferons are a family of cytokines that are antiviral and play a major role in regulating immune responses that control resistance to infection [1-3]. Alterations in interferon and other cytokine production and activity could result in changes in immunity and a possible compromise of host defenses against both opportunistic and external infections.

The purpose of the present study is to explore further the effects of space flight on cytokines and cytokine-directed immunological function.

METHODS

Among the tests carried out are interferon-alpha production, interferon-gamma production, interleukin-1 and -2 production, signal transduction in neutrophils, signal transduction in monocytes, and monocyte phagocytic activity. The experiments will be performed using peripheral blood obtained from human subjects.

In it our intent to eventually carry out these experiments using astronauts as subjects to determine the effects of space flight on cytokine production and activity. However, these subjects are not currently available. Until they become available, we will carry out these experiments using

using subjects maintained in the bed-rest model for microgravity.

RESULTS AND DISCUSSION

Over the past several years, we have been studying the effects of various factors involved in space flight on immune responses and cytokine production, in particular. We have been able to show, using a bed-rest study carried out at Johnson Space Center, showed that most cytokine parameters did not change after extended periods of bed-rest, except for interleukin-1 production. Interleukin-1 production was dramatically increased during the bed-rest period. This is an interesting observation, in that interleukin-1 is the cytokine that plays a major role in inflammation in general, but appeared to be the cytokine with major osteoclast activating activity. This suggests that alterations in immune responses as a result of bed-rest, and possibly space flight, could be related to alterations in bone and calcium metabolism. The changes induced in immune responses could play some role in inducing changes in bone, or changes in bone could play some role in inducing changes in immune responses. This could serve as a potential mechanism of induction of bed-rest, and possibly space flight, changes in immune responses.

Recently, we have continued our analysis of the bed-rest subjects. We have coordinated our findings with that of the Faculte de Medicine at Toulouse, France and have come up with the following results. We have noted that interleukin-1 not only has osteoclast activating activity, but can participate in muscle wasting often observed after cachexia. This further highlights the significance of the increase in interleukin-1 activity after bed-rest in which changes in bone and muscle were observed. Additional coordination has led to the development of a joint manuscript involving immunological results of both French and US Bed-rest studies. The coordination will allow a direct contrast of the US and French bed-rest techniques. Additional studies have been carried out using the French head-down tilt system of bed rest, and the preliminary analysis of the data look encouraging. These data are currently under analysis.

We have also carried out some studies with the head-down tilt model for rats, and stress studies correlate with the results obtained in humans.

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